

CLAIMS

1. A method of diagnosing cancer or determining p53 status in a sample suspected of being neoplastic, comprising the steps of:
- comparing the level of expression of an RNA transcript or its translation product in a first sample of a first tissue to the level of expression of the transcript or translation product in a second sample of a second tissue, wherein the first tissue is suspected of being neoplastic and the second tissue is a normal human tissue, wherein the first and second tissue are of the same tissue type, and wherein the transcript is a transcript of a gene selected from the group consisting of gene numbers 1-8, 10, 12, 14-58, 60-68, and 70-100, as shown in Figure 1;
- categorizing the first sample as neoplastic or as having a mutant p53 when expression is found to be the same or lower in the first sample than in the second sample.
2. A method of diagnosing cancer or determining p53 status in a sample suspected of being neoplastic, comprising the steps of:
- comparing the level of expression of an RNA transcript or its translation product in a first sample of a first tissue to the level of expression of the transcript or translation product in a second sample of a second tissue, wherein the first tissue is suspected of being neoplastic and the second tissue is a normal human tissue, wherein the first and second tissue are of the same tissue type, and wherein the transcript is a transcript of a gene selected from the group consisting of gene numbers 7-24, and 26-100 as shown in Figure 2;
- categorizing the first sample as neoplastic or as having a mutant p53 when expression is found to be the same or higher in the first sample than in the second sample.
3. The method of claim 1 wherein a comparison of at least two of the transcripts or translation products is performed.
4. The method of claim 2 wherein a comparison of at least two of the transcripts or translation products is performed.

5. The method of claim 1 wherein a comparison of at least five of the transcripts or translation products is performed.

6. The method of claim 2 wherein a comparison of at least five of the transcripts or translation products is performed.

5 7. The method of claim 1 wherein a comparison of at least ten of the transcripts or translation products is performed.

8. The method of claim 2 wherein a comparison of at least ten of the transcripts or translation products is performed.

10 9. The method of claim 1 wherein a comparison of at least twenty of the transcripts or translation products is performed.

10 10. The method of claim 2 wherein a comparison of at least twenty of the transcripts or translation products is performed.

15 11. The method of claim 1 wherein a comparison of at least 32 of the transcripts or translation products is performed.

12. The method of claim 2 wherein a comparison of at least 32 of the transcripts or translation products is performed.

15 13. The method of claim 1 wherein a comparison of at least fifty of the transcripts or translation products is performed.

14. The method of claim 2 wherein a comparison of at least fifty of the transcripts or translation products is performed.

20 15. The method of claim 1 wherein a comparison of 70 of the transcripts or translation products is performed.

16. The method of claim 2 wherein a comparison of 77 of the transcripts or translation products is performed.

25 17. A method of diagnosing cancer or determining p53 status in a sample suspected of being neoplastic, comprising the steps of:

comparing the level of expression of at least one RNA transcript or its translation product in a first sample of a first tissue to the level of expression of the transcripts or translation products in a second sample of a second tissue, wherein the first tissue is suspected of being neoplastic and the second tissue is a normal human tissue, wherein the first and second tissue are of the same tissue type, and wherein the

Select ~~and~~^{for} each of
a first ~~and~~^{for} ~~second~~^{and} group
group

first group of RNA transcripts consists of transcripts of genes selected from the group of genes numbered 1-8, 10, 12, 14-58, 60-68, and 70-100 as shown in Figure 1 and wherein the second group of RNA transcripts consists of transcripts of genes selected from the group consisting of genes numbered 7-24, and 25-100 as shown in Figure 2;

5 categorizing the first sample as neoplastic or as having a mutant p53 when expression of at least one of the first group of RNA transcripts or translation products is found to be the same or lower in the first sample than in the second sample, and expression of at least one of the second group of transcripts or translation products is found to be the same or higher in the first sample than in the second sample.

10 18. The method of claim 17 wherein a comparison of at least two of the transcripts or translation products in each group of transcripts or translation products is performed.

15 19. The method of claim 17 wherein a comparison of at least five of the transcripts or translation products in each group of transcripts or translation products is performed.

20. 20. The method of claim 17 wherein a comparison of at least ten of the transcripts or translation products in each group of transcripts or translation products is performed.

21. 21. The method of claim 17 wherein a comparison of at least twenty of the transcripts or translation products in each group of transcripts or translation products is performed.

25 22. The method of claim 17 wherein a comparison of at least thirty of the transcripts or translation products in each group of transcripts or translation products is performed.

23. The method of claim 17 wherein a comparison of at least fifty of the transcripts or translation products in each group of transcripts or translation products is performed.

24. The method of claim 17 wherein a comparison of at least seventy of the transcripts or translation products in each group of transcripts or translation products is performed.

30

- CONFIDENTIAL
25. The method of claim 1 wherein the level of expression of the RNA transcripts is determined using an array of nucleic acid molecules attached to a substrate in predetermined positions.
26. The method of claim 2 wherein the level of expression of the RNA transcripts is determined using an array of nucleic acid molecules attached to a substrate in predetermined positions.
- 5 27. The method of claim 17 wherein the level of expression of the RNA transcripts is determined using arrays of nucleic acid molecules attached to a substrate in predetermined positions.
- 10 28. The method of claim 1 wherein the level of expression of the RNA transcript is determined by a method comprising the steps of:
- harvesting sample mRNA from the samples;
- reverse transcribing the sample mRNA to form DNA;
- ligating a promoter to the DNA;
- 15 29. The method of claim 2 wherein the level of expression of the RNA transcript is determined by a method comprising the steps of:
- harvesting sample mRNA from the samples;
- reverse transcribing the sample mRNA to form DNA;
- ligating a promoter to the DNA;
- transcribing *in vitro* using the DNA as a template to form test mRNA;
- hybridizing the test RNA to an array of nucleic acid molecules.
- 20 30. The method of claim 17 wherein the level of expression of the RNA transcript is determined by a method comprising the steps of:
- harvesting sample mRNA from the samples;
- reverse transcribing the sample mRNA to form DNA;
- ligating a promoter to the DNA;
- transcribing *in vitro* using the DNA as a template to form test mRNA;
- hybridizing the test RNA to an array of nucleic acid molecules.
- 25 31. A method for evaluating carcinogenicity of an agent, comprising the steps of:

- contacting a test agent with a human cell;
- determining the level of expression of at least one transcript or its translation product in the human cell after contacting with the agent; wherein the transcript is of a gene selected from the group consisting of genes numbered 1-8, 10, 12, 14-58, 60-68, and 70-100 in Figure 1 and genes numbered 7-24, and 26-100 in Figure 2, wherein an agent which decreases the level of expression of a gene identified in Figure 1, or an agent which increases the level of expression of a gene identified in Figure 2 is a potential carcinogen.
- 5
32. The method of claim 31 wherein determining the level of expression of at least two of the transcripts or translation products is performed.
- 10
33. The method of claim 31 wherein determining the level of expression of at least five of the transcripts or translation products is performed.
34. The method of claim 31 wherein determining the level of expression of at least ten of the transcripts or translation products is performed.
- 15
35. The method of claim 31 wherein determining the level of expression of at least twenty of the transcripts or translation products is performed.
36. The method of claim 31 wherein determining the level of expression of at least fifty of the transcripts or translation products is performed.
37. The method of claim 31 wherein determining the level of expression of 70 of the transcripts or translation products is performed.
- 20
38. The method of claim 31 wherein determining the level of expression of 90 of the transcripts or translation products is performed.
39. The method of claim 31 wherein determining the level of expression of 100 of the transcripts or translation products is performed.
- 25
40. The method of claim 31 wherein determining the level of expression of 125 of the transcripts or translation products is performed.
41. The method of claim 31 wherein determining the level of expression of 145 of the transcripts or translation products is performed.
42. A method of treating cancer in a patient, comprising the step of:
30
administering to cancer cells of a patient a polynucleotide comprising a coding sequence of a gene selected from the group consisting of genes numbered 1-8, 10, 12,

14-58, 60-68, and 70-100 in Figure 1, wherein the cancer cells of the patient harbor a mutant p53 gene, whereby the gene is expressed in cells of the cancer.

43. A method of treating cancer in a patient, comprising the step of:

5 administering to cancer cells of a patient an antisense construct comprising at least 12 nucleotides of a coding sequence of a gene selected from the group consisting of genes numbered 7-24, and 26-100 in Figure 2, wherein the coding sequence is in 3' to 5' orientation with respect to a promoter which controls its expression, wherein the cancer harbors a mutant p53 gene; whereby an antisense RNA is expressed in cells of the cancer.

10 44. A method of screening for drugs useful in the treatment of cancer, comprising: contacting a cell which harbors a p53 mutation with a test substance;

monitoring expression of a transcript or its translation product, wherein the transcript is of a gene selected from the group consisting of genes numbered 1-8, 10, 12, 14-58, 60-68, and 70-100 in Figure 1 and genes numbered 7-24, and 26-100 in Figure 2, wherein a test substance is identified as a potential drug for treating cancer if it increases expression of a gene as shown in Figure 1 or decreases expression of a gene as shown in Figure 2.

15 45. A method of screening for drugs useful in the treatment of cancer, comprising: contacting a tumor cell which overexpresses MDM2 with a test substance;

20 monitoring expression of a transcript or its translation product, wherein the transcript is of a gene selected from the group consisting of genes numbered 1-8, 10, 12, 14-58, 60-68, and 70-100 in Figure 1 and genes numbered 7-24, and 26-100 in Figure 2, wherein a test substance is identified as a potential drug for treating cancer if it increases expression of a gene as shown in Figure 1 or decreases expression of a gene as shown in Figure 2.

25 46. A set of at least two oligonucleotide probes which hybridize to a set of p53-regulated genes, wherein the genes are selected from the group consisting of genes numbered 1-8, 10, 12, 14-58, 60-68, and 70-100 in Figure 1 and genes numbered 7-24, and 26-100 in Figure 2.

30 47. The set of claim 46 which comprises five oligonucleotide probes.

48. The set of claim 46 which comprises ten oligonucleotide probes.

- RECEIVED
U.S. PATENT AND TRADEMARK OFFICE
JULY 10 1997
49. The set of claim 46 which comprises fifteen oligonucleotide probes.
50. The set of claim 46 which comprises twenty oligonucleotide probes.
51. The set of claim 46 which comprises twenty-five oligonucleotide probes.
52. The set of claim 46 which comprises thirty oligonucleotide probes.
53. The set of claim 46 which comprises fifty oligonucleotide probes.
54. The set of claim 46 which comprises seventy-five oligonucleotide probes.
55. The set of claim 46 which comprises 100 oligonucleotide probes.
56. The set of claim 46 which comprises 140 oligonucleotide probes.
57. The set of claim 46 wherein the probes are attached to a polymer.
- 10 58. The set of claim 46 wherein the probes are attached to a solid support.
59. The set of claim 46 which comprises probes which hybridize to each of genes numbered 1-8, 10, 12, 14-58, 60-68, and 70-100 in Figure 1 and genes numbered 7-24, and 26-100 in Figure 2.
60. The set of claim 46 wherein the probes are in a gel matrix.
- 15 61. The set of claim 46 wherein the probes are in solution.
62. The set of claim 46 wherein the probes are individually packaged in a single container.
63. The set of claim 46 wherein the probes are arrayed on a solid support.
64. The method of claim 1 wherein an immunoassay is performed to determine the level of expression.
- 20 65. The method of claim 2 wherein an immunoassay is performed to determine the level of expression.
66. The method of claim 17 wherein an immunoassay is performed to determine the level of expression.